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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

IN RE: JUUL LABS, INC., MARKETING, SALES PRACTICES, AND PRODUCTS LIABILITY LITIGATION

This Document Relates to:

ALL ACTIONS

Case No. 19-md-03913-WHO

BRIEF # 3: DEFENDANT JUUL LABS, INC.'S REPLY IN SUPPORT OF OMNIBUS *DAUBERT* MOTION TO EXCLUDE CERTAIN OPINIONS ON TOXICITY AND ALLEGED HEALTH EFFECTS

Judge: Hon. William H. Orrick
Date: February 25, 2022
Courtroom: 2

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INTRODUCTION

Plaintiffs' response does not directly address the significant methodological shortcomings present in their experts' general and specific causation opinions. Instead, Plaintiffs mischaracterize JLI's arguments and attempt to relax *Daubert*'s requirements on causation. Plaintiffs' consistent refrain is that *Daubert* allows everything but "junk science" to be presented to the jury. Not so. An expert's opinion must be based upon a reliable scientific methodology, and the experts' opinions here do not meet that standard. As to general causation, Plaintiffs' experts do not properly account for dose or exposure, both of which are required under Ninth Circuit law. As to specific causation, the experts' opinions fall short because the experts did not employ differential diagnosis or any other reliable methodology to rule out other potential causes of B.B.'s alleged injuries, and they lack any reliable basis to opine that B.B. actually suffered from the myriad injuries she claims.

Plaintiffs also suggest that JLI's arguments are best left to the jury as they raise competing interpretations of science. Again, not so. JLI's *Daubert* motion is based on the methodological limitations and the dearth of scientific evidence supporting Plaintiffs' experts' opinions. This is not a matter of disputed science.

For these reasons and those stated in JLI's opening brief, JLI respectfully requests the Court exclude (i) expert opinions that JUUL, its chemical constituents, or nicotine in JUUL are toxic; (ii) expert opinions on general causation for non-addiction health claims; (iii) expert opinions about the impact of nicotine on the developing brain or the psychological impact of addiction, and (iv) expert opinions on specific causation for B.B.'s non-addiction claims and medical monitoring damages. *See* Appendix A.

I. PLAINTIFFS' RECITATION OF *DAUBERT* LAW ON CAUSATION IGNORES ITS REQUIREMENTS.

While Plaintiffs contend in their response that the standard of admissibility for expert testimony is "liberal" and "favor[s] admission," Pls. Br. at 103 (*citing In re Roundup Prods. Liab. Litig.*, 390 F. Supp. 3d 1102, 1112 (N.D. Cal. 2018)), even a liberal standard is still a standard. Plaintiffs' recitation of the law incorrectly minimizes *Daubert*'s requirements that Plaintiffs' experts must have a sufficiently reliable methodology and scientific basis to opine on either general or specific causation.

A. General Causation

Plaintiffs do not dispute that to establish general causation, the generally accepted methodology begins with looking for a statistically significant association between exposure and injury. JLI Br. #3 at 2. Indeed, as even the case cited by Plaintiffs acknowledges, "epidemiology is central to the general causation inquiry." *In re Roundup*, 390 F. Supp. 3d at 1116. *See also, e.g.*, *Hardeman v. Monsanto Co.*, 997 F.3d 941, 963 (9th Cir. 2021) ("Here, Hardeman's general causation experts relied on three types of studies: epidemiological, animal, and cellular.")) Plaintiffs also do not seriously dispute that an association is not equal to evidence of causation, or that expert testimony based solely on animal studies (absent some reason to extrapolate to humans), anecdotal evidence, biological plausibility, or temporal relationships does not meet *Daubert*'s standards.

Plaintiffs' response instead makes various arguments that improperly attempt to relax *Daubert*'s standards or create a strawman. *First*, Plaintiffs argue that expert opinions on causation need not be established to a high degree of certainty to be admissible. Pls. Br. at 103, 105. JLI never argued in its opening brief that complete certainty was required.[1] Instead, JLI argued that Plaintiffs' experts did not employ reliable scientific methodology or use reliable scientific evidence to reach their opinions. *Daubert* may not require certainty, but it requires more than the guesswork, speculation, and unsupported leaps of logic employed by Plaintiffs' experts here.

Second, Plaintiffs argue in various ways that experts may permissibly opine on causation based on an examination of "the totality of scientific evidence," and that there is no "magic formula" to be followed. Pls. Br. at 103-04. Again, JLI never contended that an expert could not draw an opinion from the totality of the scientific evidence; indeed, an expert should review all available scientific evidence on a topic prior to drawing a conclusion on causality. The problem for Plaintiffs is there is no reliable scientific evidence supporting their methodology or allowing them to draw the conclusions that they attempt to reach here.

Third, Plaintiffs contend that experts may disagree and competing expert opinions should be left for the jury's consideration. Pls. Br. at 103-04. JLI does not disagree with these unremarkable

[1] Plaintiffs cite *Kennedy v. Collagen Corp.*, 161 F.3d 1226, 1230 (9th Cir. 1998) and *Primiano v. Cook*, 598 F.3d 558, 563 (9th Cir. 2010), *as amended* (Apr. 27, 2010). *Kennedy* does not save Plaintiffs for the reasons stated *infra*. *Primiano* is also inapt, as the question there was why a specific patient's elbow replacement failed so quickly—which is decidedly not a complicated issue of general causation. 598 F.3d at 563.

propositions, but its *Daubert* motion was not based upon the fact that its experts may disagree with Plaintiffs' experts.

Finally, none of the three cases discussed in Plaintiffs' response establish that JLI's recitation of *Daubert* law was incorrect. Pls. Br. at 105-06. Plaintiffs rely on *Wendell v. GlaxoSmithKline LLC* for the proposition that expert evidence can be admitted without epidemiology. That case, however, dealt with an "exceedingly rare cancer, with only 100 to 200 cases reported since it was first recognized," and the court noted that "it is not surprising that the scientific community has not invested substantial time or resources into investigating the causes of such a rare disease." 858 F.3d 1227, 1236 (9th Cir. 2017). None of Plaintiffs' alleged injuries are of the variety that is too rare to be studied by the scientific community. In *Kennedy*, the expert's opinion—in the absence of epidemiology—was based upon peer-reviewed publications and "clinical trials and product studies conducted by the defendant." 161 F.3d at 1228. And unlike *In re Roundup*, Plaintiffs do not offer statistically significant epidemiology evidence of an association that is simply "open to different interpretations." 390 F. Supp. 3d at 1126. Plaintiffs here do not even reach the first hurdle of establishing a statistically significant association, a prerequisite to application of the Bradford Hill criteria. *Id*. at 1130; Reference Manual at 295-99.

B. Specific Causation

As with their recitation of *Daubert* law applicable to general causation, Plaintiffs' argument on specific causation seeks to minimize *Daubert*'s requirements in a manner wholly inconsistent with Ninth Circuit law. Plaintiffs are incorrect that JLI seeks to apply "heightened legal and scientific standards." Pls. Br. at 123. Rather, it is Plaintiffs who seek to disregard governing Ninth Circuit law that requires experts offering specific causation opinions to consider and rule out potential alternative causes of an alleged injury, including through differential diagnosis methodology. JLI Br. #3 at 6-7 (citing cases). Even the cases that Plaintiffs cite recognize this. In *Messick v. Novartis Pharms. Corp.*, the expert physician conducted a differential diagnosis relying on his "extensive clinical experience" and a recognized diagnostic definition. 747 F.3d 1193, 1198 (9th Cir. 2014). While the Ninth Circuit stated that "we do not require that an expert be able to identify the sole cause of a medical condition," it recognized the expert "must provide scientifically sound reasons for excluding potential causes." *Id.* at 1198-99. Likewise, in *Clausen v. M/V New Carissa*, the Ninth Circuit held the expert's differential

diagnosis used a scientifically sound methodology to rule in and then rule out potential causes.[2] 339 F.3d at 1061. In *Wendell*, the expert physicians performed differential diagnoses; indeed, one expert testified "he performs differential diagnosis in attempting to diagnose every patient, and that he has applied the same technique [in *Wendell*] to determine the cause of a disease." 858 F.3d at 1234-35. And in *In re Roundup Prods. Liab. Litig.*, the experts used differential diagnosis and ruled out that plaintiffs had "other significant risk factors" for the alleged injuries. 358 F. Supp. 956, 959-60 (N.D. Cal. 2019).

II. PLAINTIFFS HAVE FAILED TO EMPLOY WELL-ESTABLISHED, RELIABLE METHODS IN THEIR OPINIONS REGARDING NON-ADDICTION HEALTH RISKS.

Plaintiffs claim their experts confirmed a positive association between JUUL and lung injury, and then applied the Bradford Hill criteria to establish causation. Pls. Br. at 106. However, Plaintiffs' experts offer no methodology to bridge the gap between the studies they cite, which examine ENDS generally, and their conclusions about JUUL specifically.[3] Plaintiffs' claim that epidemiological studies establish a positive association between JUUL aerosol and pulmonary injury is false: none of the studies cited by Tackett or Pue examine JUUL aerosol. Instead, Tackett and Pue rely on studies that assess the possible connection between ENDS generally and lung injuries. Crucially, Tackett and Pue do not explain how the general ENDS studies translate to JUUL specifically, which is an essential step in establishing causation given that Tackett admitted JUUL produces much lower levels of potentially toxic carbonyls than other types of ENDS products. Ex. 53, Tackett Dep. 118:1–20, 257:13–18. Plaintiffs also reference animal studies, chemical analyses, and personal observations as evidence supporting causation, but do not dispute that those forms of evidence are less scientifically reliable than epidemiology. Moreover, those lesser forms of evidence cannot establish causation absent a detailed analysis extrapolating the results to ordinary JUUL use in humans, which Plaintiffs' experts do not perform. *See, e.g.*, *Newkirk v. ConAgra Foods, Inc.*, 727 F. Supp. 2d 1006, 1026 (E.D. Wash. 2010), aff'd, 438 F. App'x 607 (9th Cir. 2011)

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[2] Plaintiffs' argument that the *Clausen* court upheld admission of expert testimony even though "neither of *Daubert II*'s primary criteria for establishing the reliability of expert testimony is met in this case" is a strawman. Pls. Br. at 124. JLI never argued that Plaintiffs' experts should not be admitted because the opinions were not made independent of the litigation and were not subject to peer review. *Clausen*, 339 F.3d at 1056.

[3] Plaintiffs misconstrue two statements from JLI's PMTA regarding the potential respiratory consequences of ENDS as JLI's admissions about its product. Pls. Br. at 106. However, those quotes refer to ENDS generally, not JUUL specifically, and do not constitute any admission about JUUL products. Pls. Ex. 43, JLI20002862.

(excluding expert testimony because the expert offered "no explanation for how and why the results of those studies can be extrapolated to humans"). Accordingly, Plaintiffs' experts fail to demonstrate a statistically significant association, without which they cannot establish causation via the Bradford Hill criteria. *See, e.g.*, Reference Manual at 598–99 (the Bradford-Hill criteria "are employed only after a study finds an association to determine whether that association reflects a true causal relationship").

Even if Plaintiffs' experts had adequate evidence of a positive association between JUUL use and lung injuries, which they do not, their application of the Bradford Hill criteria does not make the requisite leap from association to causation. Tackett, for example, simply lists the Bradford Hill criteria, provides a brief description of each, states he addresses them "in depth above," and concludes that (apparently all of) the factors are "clearly met." Ex. 24, Tackett Rep. 55–56. He does not explain which studies or data support which factors, nor does he offer analysis explaining why any of the factors are met. Ex 53, Tackett Dep. 231:5–9. Moreover, despite listing hundreds of studies in their reliance lists, Tackett and Pue cannot point to a single example that finds JUUL specifically, or even ENDS generally, causes lung injury. Where in an area of significant study, there is no opinion by anyone other than the experts at issue supporting general causation, "[t]he unavoidable conclusion is that their weighing of the Bradford Hill factors does not represent a faithful application of an accepted methodology." *In re Viagra (Sildenafil Citrate) & Cialis (Tadalafil) Prods. Liab. Litig.*, 424 F. Supp. 3d 781, 798–99 (N.D. Cal. 2020). Tackett's and Pue's unsupported recitations of Bradford Hill criteria are not sufficient to establish general causation.

A. Plaintiffs Fail to Establish General Causation Based on Epidemiology, Toxicology, or Any Other Reliable Methodology.

Epidemiology is the primary generally accepted method for demonstrating general causation. *In re Lipitor (Atorvastatin Calcium) Mktg., Sales Pracs. & Prods. Liab. Litig.*, 174 F. Supp. 3d 911, 926 (D.S.C. 2016). Every one of the epidemiological studies cited by Tackett and Pue in their respective reports evaluates ENDS generally, not JUUL specifically.[4] Moreover, none of the studies concludes there is a causal association between ENDS use and respiratory disease. Wills et al. (2021), the only

[4] Notably, the epidemiological citation on which Tackett and Pue rely almost exclusively, Wills et al. (2021), relies in significant part on data that pre-date JUUL's launch in mid-2015. Pls. Ex. 26, Wills et al., *E-cigarette Use and Respiratory Disorders: An Integrative Review of Converging Evidence from Epidemiological and Laboratory Studies*, Eur Respir. J., 57:1901815 (2021).

epidemiological study discussed in detail in either report, concluded only that evidence supports "a real relationship between e-cigarettes and respiratory disorders." Pls. Ex. 26, Wills et al., *E-cigarette Use and Respiratory Disorders: An Integrative Review of Converging Evidence from Epidemiological and Laboratory Studies*, Eur Respir. J., 57:1901815 (2021). Concluding that a causative relationship exists based on a study that examines non-JUUL products and asserts "a real relationship" is a quintessential example of an unjustified leap in logic meriting exclusion. *See In re Roundup*, 390 F. Supp. 3d at 1134 (citing *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)) ("The Court must also assure itself that the expert's conclusions are not based upon unreasonable extrapolations from the existing data."). Further, Wills et al. noted it was still unclear "whether e-cigarette use is more related to onset of disease or to exacerbation of existing symptomatology," and confirmed "further research is needed to solidify knowledge about the health consequences of e-cigarettes." Wills et al. (2021) at 11–12. In addition, while the authors generally attempt to distinguish between current smokers and non-smokers of combustible cigarettes, they do not appear to account for former smokers, which would certainly influence the results. *Id.* The lack of clarity and limitation on data has been identified by public health experts, who note that "[h]igh-quality clinical and epidemiological data on vaping's health effects are relatively sparse. There are no data on long-term health effects, reflecting the relative novelty of vaping and the rapid evolution of vaping products. Determining even short-term health effects in adults is difficult because most adult vapers are former or current smokers. Balfour et al., *Balancing Consideration of the Risks and Benefits of E-Cigarettes*, Am. J. Pub. Health 111, 1661–72 (2021), https://pubmed.ncbi.nlm.nih.gov/34410826/.

Tackett admits other ENDS products can produce higher levels of carbonyls than JUUL due to JUUL's unique temperature regulation system, yet neither Dr. Tackett nor Dr. Pue explain how the results of the epidemiological studies of ENDS generally would apply to JUUL given its lower carbonyl levels. Ex. 53, Tackett Dep. 117:18–118:20, 257:13–18.[5] Indeed, contrary to Plaintiffs' assertions, Tackett

[5] In their Opposition, Plaintiffs reference Chaffee et al. (2021), which found elevated respiratory risks "regardless of the device type used." This characterization is misleading. Neither Tackett nor Pue discuss the merits of Chaffee in their reports—both merely cite it (incorrectly spelled "Chafee" in both reports) in identical string cites of epidemiological studies that they claim suggest a positive association. Ex. 24, Tackett Rep. 54; Ex. 21, Pue Rep. 23. More importantly, Chaffee et al. does not distinguish JUUL from other ENDS devices. Instead, it lumps JUUL in with other pod devices, including "pod-mods" and "other rechargeable pod devices." Chaffee et al. (2021) at 4. Chaffee does not account for JUUL's unique temperature control system, which produces lower levels of carbonyls than other devices, negating its purported usefulness as a bridge between ENDS and JUUL.

stated, "comparison to other nicotine delivery devices, for purposes of my report are irrelevant." Ex. 24, Tackett Rep. 41. Tackett and Pue did not account for the differences between JUUL and other ENDS products in reaching their conclusions, and therefore cannot make reliable pronouncements on JUUL's toxicity based on epidemiological data. Tackett and Pue also rely on other forms of less reliable data, including animal, cellular, and aerosol studies, but likewise fail to offer adequate methodology to establish general causation.

1. Plaintiffs Do Not Properly Consider Dose.

Plaintiffs assert their experts need not demonstrate that any constituents are present in JUUL aerosol in toxic doses. Pls. Br. at 110.[6] Plaintiffs are wrong. Dose matters in any evaluation of toxicity, as virtually all substances become toxic at high enough levels. *See* Reference Manual at 636 ("[A]ll chemical agents are intrinsically hazardous—whether they cause harm is only a question of dose. Even water, if consumed in large quantities, can be toxic."). Perhaps Plaintiffs would have a point if they could reliably establish through epidemiological studies that use of JUUL causes lung injury—as noted above, they cannot. Instead, they attempt to establish that certain constituents in JUUL aerosol cause harm.

a. Plaintiffs' Experts Fail to Establish That Exposure to JUUL Aerosol Is Toxic.

The simplest way for Plaintiffs' experts to establish the toxicity of a specific chemical in JUUL would be to determine the toxic threshold of the chemical, then demonstrate that a user's exposure to that chemical through JUUL use is above the threshold. Plaintiffs concede they cannot establish threshold doses, so this option is unavailable. Pls. Br. at 110. Alternatively, Plaintiffs' experts could directly prove that exposure to the chemical or compound in the amount it is present in JUUL aerosol is toxic. Plaintiffs' experts fail to do this as well. Instead, they simply conclude certain chemicals detected in JUUL can be toxic without establishing they are toxic at doses present in JUUL products.

[6] Plaintiffs cite *Clausen v. M/V New Carissa*, 339 F.3d 1049 (9th Cir. 2003), for this argument. *Clausen* examined whether an expert could factor in toxic effects of oil as a potential cause of oyster mortality when performing a differential diagnosis, where no minimum quantity of oil was established to cause harm to gill feeding organisms. *Id.* at 1059. Unlike Tackett and Pue, the expert in *Clausen* conducted his own lab examinations of the impacted population to rule in oil contact toxicity as a possible cause of morbidity. *Id.* *Westberry v. Gislaved Gummi AB*, 178 F.3d 257, 264 (4th Cir. 1999), another case cited by Plaintiffs, examined whether exposure to high levels of talc could be ruled in for a differential diagnosis of a specific individual's sinus condition. *Id.* at 264. Neither of these cases involved sweeping, unsupported generalizations like those proffered by Tackett and Pue.

Plaintiffs attempt to divert attention from their inadequate methodology by erroneously claiming JUUL is akin to a pharmaceutical drug in that there is no background exposure to compare against, rendering establishment of toxic dose unnecessary. Pls. Br. at 111–12. Plaintiffs' reliance on *In re: Zicam Cold Remedy Mktg., Sales Pracs., & Prods. Liab. Litig.*, 797 F. Supp. 2d 940 (D. Ariz. 2011), however, does not save their experts. In *Zicam*, although Plaintiffs were not required to prove toxic dosage on summary judgment, they were required to demonstrate the drug at issue "is toxic to humans given substantial exposure." *Id*. at 946. Moreover, the distinguishing factor in Zicam was that the general population's level of exposure to the constituent at issue, zinc gluconate nasal ingestion, was zero—no background exposure whatsoever. *Id*. By contrast, Tackett testified that many of the chemicals in JUUL that he identified as being sources of harm (including formaldehyde, acetaldehyde, and acrolein) are present in background levels in the air people breathe every day. Ex. 53, Tackett Dep. 124:6–125:16. This is not a case alleging exposure to a unique pharmaceutical chemical that is absent from other products or aspects of daily life (in which case it would perhaps not be as meaningful to establish a toxic threshold). Chemicals found in JUUL aerosol are also present in other everyday products—including combustible cigarettes, which JUUL is intended to replace. *Zicam* does not obviate the need for Plaintiffs' experts to establish toxicity at JUUL doses.

Plaintiffs also attempt to circumvent the low doses of allegedly toxic chemicals in JUUL by asserting it is the specific combination of chemicals in JUUL, not each chemical individually, that must be assessed for toxicity. Pls. Br. at 112. But the studies and data Tackett and Pue rely on address the toxicity of either (1) ENDS generally or (2) particular constituents, not JUUL aerosol specifically. There is no data supporting that JUUL aerosol is toxic "at the level of exposure alleged by plaintiffs," which is the required standard in the Ninth Circuit. *See In re Hanford Nuclear Rsrv. Litig.*, 292 F.3d 1124, 1133 (9th Cir. 2002); *see also In re Bextra & Celebrex Mktg. Sales Pracs. & Prod. Liab. Litig.*, 524 F. Supp. 2d 1166, 1174 (N.D. Cal. 2007) ("The Court finds that dose matters" in a pharmaceutical drug case.).

b. Plaintiffs' Experts Fail to Establish That Certain Constituents Are Present in JUUL Aerosol at Toxic Levels.

Despite their claim that the complex combination of constituents in JUUL aerosol is what is really at issue, Plaintiffs' experts nevertheless examine and characterize specific constituents as being the cause of harm. Plaintiffs effectively concede their experts do not consider dose for any chemical in JUUL other than vanillin, diacetyl, and methylglyoxal. But Tackett and Pue do not reliably establish that any of these constituents are present in JUUL aerosol at a harmful level. For vanillin, Tackett cites a study that found vanillin in Crème Brulee aerosol, but offers no calculations or other methodology comparing the levels in the study to the purported occupational limit for vanillin. Ex. 24, Tackett Rep. 21. Instead, he simply concludes the study "rais[es] the question" of what long-term effects inhalation of vanillin via JUUL aerosol may have. *Id*. In order to establish that the vanillin in JUUL is toxic, Tackett would need to take the extra step of examining how the level found in JUUL compares with the occupational limit. He does not do so. For diacetyl, Tackett extrapolates a short-term exposure limit from 8-hour occupational exposure limits, but does not compare it with the levels of diacetyl found in JUUL aerosol and does not assert that typical JUUL use would expose a user above that limit. *Id.* 25. For methylglyoxal, Tackett calculates a recommended exposure limit based on the diacetyl limit, but his calculation is based on unreliable and inapplicable assumptions. Specifically, Dr. Tackett bases his assumption that methylglyoxal "is even more toxic than diacetyl at lower levels," which is critical to his calculations, on Hubbs et al. (2019). Hubbs et al., *Flavorings-Related Lung Disease: A Brief Review and New Mechanistic Data*. Toxicol Pathol. 2019 Dec; 47(8):1012-1026, https://pubmed.ncbi.nlm.nih.gov/31645208/. However, Hubbs et al. is an animal study that measures levels of methylglyoxal and diacetyl far above the levels found in JUUL aerosol. Ex. 53, Tackett Dep. 193:3–195:5. Tackett does not extrapolate this data to humans at the levels found in JUUL aerosol, and therefore misses a critical step necessary to establish general causation. *See Newkirk*, 727 F. Supp. 2d at 1026. Tackett also relies on Azimi et al. to establish the actual amount of methylglyoxal in JUUL aerosol, the other essential basis for his calculations. Azimi et al., *An Unrecognized Hazard in E-Cigarette Vapor: Preliminary Quantification of Methylglyoxal Formation from Propylene Glycol in E-Cigarettes*, Int. J. Environ. Res Public Health 2021, 18, 385, 2020, https://pubmed.ncbi.nlm.nih.gov/33419122/. But some of the JUULpods Azimi et al. tested were obtained

from an unauthorized reseller and may have been counterfeit, which Tackett admits could mean the results are not reflective of authentic JUUL products. Ex. 53, Tackett Dep. 212:4–11. Plaintiffs' experts fail to reliably establish that any constituent is present at a harmful dose in JUUL aerosol.

In support of their "additive effect" claim—which is used as a crutch in Tackett's and Pue's reports to inexplicably thrust non-toxic doses of constituents in JUUL into the sphere of toxicity—Plaintiffs reference benzoic acid as enabling toxins to reach deep into the lungs, and methylglyoxal as inhibiting metabolism of formaldehyde, thereby rendering it more hazardous. Pls. Br. at 114. However, Tackett never explains how benzoic acid's effect correlates to increased harm. In addition, Plaintiffs' experts do not assert that the level of formaldehyde measured in JUUL aerosol exceeds established toxic threshold levels, whether combined with methylglyoxal or not. Rather, Tackett concedes formaldehyde levels in JUUL are below toxic thresholds, but claims those thresholds may be inappropriate for a complex mixture of chemicals like JUUL. Ex. 24, Tackett Rep. 4, 28. But he does not offer further explanation or attempt to calculate what he considers an appropriate threshold to establish formaldehyde in JUUL is toxic. Plaintiffs' experts have not provided any scientifically reliable evidence that the combination of chemicals in JUUL aerosol render it more hazardous than each chemical would be individually.

2. Following the PMTA Process Ensures Reliability and Plaintiffs' Experts Ignored It.

Plaintiffs complain that following the PMTA process is not a requirement under *Daubert*. Pls. Br. at 115. Although *Daubert* does not mandate following the PMTA process per se, *Daubert* requires reliability, and that's exactly what the PMTA's risk assessment entails. No expert finds that the PMTA process was unreliable. Plaintiffs experts chose to rely upon unreliable nonclinical studies that contrast those detailed in the PMTA. Plaintiffs also criticize JLI's risk assessment as not comprehensive because JLI did not include the toxic effects of certain chemicals. Pls. Br. at 115. [redacted] Plaintiffs' experts' failure to follow the PMTA process in assessing the harms of the product renders their opinions unreliable and does not simply go to the weight of the opinions.

3. Plaintiffs' Experts Have Failed To Present Reliable Scientific Evidence Regarding Nicotine Toxicity.

JLI's position is not that nicotine is safe, but rather that there is no reliable evidence that the level of nicotine in JUULpods is toxic or causes chronic health effects. Plaintiffs contort the issue to focus instead on the effects of exposure to enormous amounts of nicotine. The central issue, which Plaintiffs again fail to grasp, is dose. Plaintiffs repeatedly state nicotine can be acutely toxic "in large doses," but do not explain what a "large dose" is, nor do they suggest that JUUL use exposes people to "large doses."[7] The fact that nicotine can become toxic at a dose far higher than what is present in JUUL is irrelevant and cannot form the basis of a reliable expert opinion on the toxicity of nicotine in JUUL. Plaintiffs offer no evidence or methodology demonstrating that acute nicotine toxicity is associated with, much less caused by, JUUL use.

Plaintiffs begin their toxicity argument by noting that nicotine is a naturally occurring insecticide "secreted by plants in the nightshade family"—which, in addition to tobacco leaves, includes tomatoes, eggplants, and potatoes. Many household items, including toothpaste and antibacterial soap, can contain chemicals that are natural pesticides. But that does not mean toothpaste and antibacterial soap cause harm to humans when used at reasonable doses. The same applies to the nicotine in JUUL.

Plaintiffs reference Grunberg's citation to Bernd Mayer to establish nicotine can be lethal to humans. *See* Ex. 8, Grunberg Rep. 16 (citing Bernd Mayer, *How Much Nicotine Kills a Human? Tracing back the generally accepted lethal dose to dubious self-experiments in the nineteenth century*, Arch Toxicol (2013), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3880486/). Again, that is immaterial absent some connection to the nicotine concentration in JUUL. Moreover, Bernd Mayer identifies a discrepancy between the long-established lethal dose of nicotine for adults of 60 mg and published cases of nicotine intoxication: If the lethal dose were as low as the traditional calculation, there would be far more published cases of nicotine toxicity. *See* Bernd Mayer. Bernd Mayer concludes, "[T]he frequent warnings of potential fatalities caused by ingestion of small amounts of tobacco products or diluted

[7] Following Plaintiffs' logic, water is also "toxic" because it can become toxic at high enough doses. *See* Reference Manual at 636 ("[A]ll chemical agents are intrinsically hazardous—whether they cause harm is only a question of dose. Even water, if consumed in large quantities, can be toxic.").

nicotine-containing solutions are unjustified and need to be revised in light of overwhelming data indicating that more than 0.5 g of oral nicotine is required to kill an adult." *Id*. Certainly, Plaintiffs cannot suggest JUUL users are exposed to anywhere near 500 mg of nicotine—which would be equivalent to simultaneously ingesting more than a dozen JUUL pods—through normal use.

In addition, Plaintiffs claim the 2014 and 2016 Surgeon General Reports conclude that nicotine consumption by adolescents can create lasting damage to "overall health." But neither Report makes such a broad pronouncement about the effects of consumption of nicotine on "overall health." Plaintiffs further note that the 2014 and 2016 Reports conclude that nicotine consumption by adolescents can create lasting damage to brain development.[8] But JLI is not suggesting that JUUL products are safe for youth; to the contrary, JLI maintains that its products are appropriate for adult use only. Plaintiffs also recite the purported nicotine warning on Altria's ENDS product as evidence that nicotine is toxic, but that information is immaterial to an examination of nicotine in JUUL products and should be disregarded.

To be clear, JLI is not claiming nicotine is safe or that it does not carry risk. Rather, as noted in Fagerström, "[o]ver the last 50 years, the concept of tobacco harm reduction has been well established," and "[i]t is now understood that nicotine itself is not very harmful." Pls. Ex. 48, Fagerström & Bridgman, *Tobacco Harm Reduction*, 39 Addictive Behaviors 507. Nor is JLI's position extreme. Indeed, myriad studies have been conducted that support that nicotine is not as harmful as Plaintiffs contend. Regarding acute toxicity, human studies indicate, "[n]icotine is hardly ever the cause of serious and fatal poisonings." Sommerfeld et al., *Intravenous and oral suicidal e-liquid poisonings with confirmed nicotine and cotinine concentrations*, Forensic Science International, 262, e15-e20 (2016), https://pubmed.ncbi.nlm.nih.gov/27020616/. Regarding immunotoxicity, "[i]t appears on balance that nicotine is not a major contributor to the chronic inflammatory state caused by smoking." Benowitz & Burbank, *Cardiovascular toxicity of nicotine: Implications for electronic cigarette use*, Trends in Cardiovascular Medicine, 26(6), 515-523 (2016), https://pubmed.ncbi.nlm.nih.gov/27079891/. Regarding cardiovascular disease, studies demonstrate no association between sustained NRT use and the

[8] While the 2016 Report draws this conclusion, the 2014 Report actually concludes the evidence "is suggestive" that adolescent nicotine exposure "may have" adverse consequences for brain development. Surgeon General's Report, 2014 at 8.

occurrence of cardiovascular disease. Murray et al., *Does nicotine replacement therapy cause cancer? Evidence from the Lung Health Study*, Nicotine & Tobacco Research, 11(9), 1076-1082 (2009), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2725009/; Murray et al., *Safety of Nicotine Polacrilex Gum Used by 3,094 Participants in the Lung Health Study*, Chest, 109(2), 438-445 (1996), https://pubmed.ncbi.nlm.nih.gov/8620719/. Further, increases in nicotine, such as by adding nicotine medication in a smoker, show no increase in cardiovascular effects, including heart rate or catecholamine release. Benowitz, *Pharmacology of Nicotine: Addiction, Smoking-Induced Disease, and Therapeutics*, Annual Review of Pharmacology and Toxicology, 49(1), 57-71 (2009); Benowitz, & Gourlay, *Cardiovascular Toxicity of Nicotine: Implications for Nicotine Replacement Therapy*, Journal of the American College of Cardiology, 29(7), 1422-1431 (1997), https://pubmed.ncbi.nlm.nih.gov/9180099/.

Plaintiffs are correct that Zeller suggested a reduction of nicotine in combustible cigarettes could prove beneficial to public health—not because nicotine is harmful, but because reducing addictiveness could reduce consumption of other constituents of combustible cigarettes that are harmful. Pls. Ex. 49, Zeller & Gottlieb, *A Nicotine-Focused Framework for Public Health*, 377 New England J. Medicine 1111 (2017). Indeed, Plaintiffs do not dispute that the decades of deaths, lung diseases, and other harms attributable to smoking do not come from the nicotine, but from the tar in combustible cigarettes. *See* M. A. H. Russell, *Low-Tar and Medium-Nicotine Cigarettes*, British Medical Journal 1430, 1431 (1976), https://www.jstor.org/stable/20410158 ("People smoke for nicotine but they die from the tar."). Plaintiffs also do not dispute their own expert Casey's admission that the majority of study on nicotine is performed in the context of combustible cigarettes. Ex. 1, Casey Rep. 10. Plaintiffs, like their experts, often fail to distinguish between the effects of combustion and nicotine itself.

Plaintiffs concede that their experts did not conduct a Bradford Hill analysis to examine whether the studies they cite meet the criteria to establish general causation. Nor do they address JLI's specific challenges to their experts' analysis of the acute and chronic effects of nicotine. *See* JLI Br. #3 at 15–16. Instead, Plaintiffs simply reference two pages of Grunberg's report and assert their experts' opinions are (apparently all) based on "the totality of the studies." *See* Pls. Br. at 118. But their experts do not synthesize the studies they cite or analyze what "the totality" reliably demonstrates about the potential harms of nicotine in JUUL products. In the two pages of his report that Plaintiffs cite, Grunberg asserts a

rapid-fire string of conclusory statements about nicotine, each of which contains one or zero citations to purported evidentiary support. *See* Pls. Br. at 118. Grunberg does not identify which of these studies examine ENDS, JUUL, combustible cigarettes, or nicotine alone. Ex. 8, Grunberg Rep. 16–17. Nor does Grunberg specify whether the studies were conducted on humans, animals, or cells, much less whether the studies are reliable or how they could be extrapolated to draw conclusions about risks to humans using JUUL. *Id*. That analysis is required to establish causation, and without it, Plaintiffs' experts' scattershot opinions about nicotine toxicity must be excluded. *See In re Bextra*, 524 F. Supp. 2d at 1175 ("[T]he general causation inquiry is whether exposure to the challenged substance '*at the level of exposure alleged by the plaintiffs* is capable of causing a particular injury or condition in the general population.'") (quoting *In re Hanford*, 292 F.3d at 1133) (emphasis in original); *Newkirk*, 727 F. Supp. 2d at 1026 (excluding expert testimony because the expert offered "no explanation for how and why the results of those studies can be extrapolated to humans").

4. Determining the Impact of the JUUL Product on Baseline Consumer Risk Is a Matter of Reliability, Not Weight.

Plaintiffs contend their experts are not required to compare JUUL harms to the baseline consumer risk presented to smokers, former smokers, and nicotine naïve users and that their failure to do so concerns the weight to be given to their opinions. Pls. Br. at 118-19. The TCA and FDA say otherwise. The TCA and FDA instruct that relevant standard for ENDS products is "appropriate for the protection of public health"—not safe and effective. *See* 21 U.S.C. § 387j(c)(2)(A). This requires an assessment of both the risks and the benefits of the product. *See* Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems: Guidance for Industry. June, 2019. Silver Spring, MD: U.S. Dept. of Health and Human Services—Food and Drug Administration (FDA)—Center for Tobacco Products, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/premarket-tobacco-product-applications-electronic-nicotine-delivery-systems-ends. For Plaintiffs' experts to opine that JUUL is not safe, without comparing it to combustible cigarettes, is essentially a half-baked analysis. While Plaintiffs argue that they need not do so, because selling a product that is "less hazardous" than combustible cigarettes is "not saying much," they lose sight of the regulatory environment in which JLI operates. Pls. Br. at 106. The FDA recognizes through its appropriate for the protection of public health

standard that any alleged health effects from using JUUL products must be understood in relation to the health risks from using other tobacco products like combustible cigarettes. The critical question, as JLI has explained, is not whether using JUUL may pose health risks in a vacuum; it is whether using JUUL products decreases risk compared with smoking combustible cigarettes. Plaintiffs' experts fail to address that crucial comparison and fail in their opposition to put forth any legal authority to excuse their failures to assess the baseline consumer risk of JUUL.

B. Plaintiffs' Response Confirms Their Experts' Non-Addiction Opinions Are Not Based Upon Reliable Scientific Evidence.

1. Seizures and EVALI.

Plaintiffs contend that the Parties agreed that "any issue with expert testimony regarding JUUL's [sic] generally causes seizures or [e-cigarette or vaping associated lung injury ('EVALI')] should be deferred until a bellwether plaintiff intends to offer such evidence at trial" and thus "the Court need not address these issues at this time." Pls. Br. at 119. Not so. Defendants have twice informed Plaintiffs that this statement is incorrect: there was no agreement between the Parties that these issues should be deferred. Indeed, at the December 5, 2021 Case Management Conference, Plaintiffs stated to the contrary: "We'd rather just get the issues resolved. If they have serious challenges to our experts that we might call in our personal injury cases, let's get them heard now." December 6, 2021 CMC Hr'g Tr. at 39:6-8.

Plaintiffs have put these conditions at issue in both their case-specific and generic pleadings and expert reports. Both upcoming bellwether cases—Bain and Pesce—generally allege the use of JUUL causes or increase the risk of seizures and EVALI. *See* Bain Second Am. Compl. ¶¶ 11, 218, 723-30, 738-42, 763-64, 783, 785, 794, 816, 834, 836, 842, 866, 872, 884, 930, 1024, 1027; *see also* Pesce Am. Compl. ¶¶ 11, 218, 723-30, 738-42, 765-66, 786, 788, 800, 827, 833, 827, 833, 837, 854, 878, 891. And in their reports and depositions, Plaintiffs' experts opine on JUUL as a cause of or risk for seizures, *see, e.g.*, Ex. 25, Winickoff Rep. 13 ("Recent case reports have confirmed an elevated risk of seizures with e-cigarette use."), Ex. 11, Jackler Rep. 317 ("Some teens have gone so far as to trigger seizures due to nicotine overdose using JUUL."); Ex. 16, Noar Rep. 46 ("WARNING: Exposure to e-liquids from drinking, eye contact, or dermal contact can result in vomiting or seizures."), as well as EVALI, *see, e.g.*,

[redacted]

[redacted] Ex. 1, Casey Rep. 30–31 ("[I]t is my opinion that EVALI can also occur in patients whose vape exposure was exclusively nicotine, such as JUUL."); Ex. 8, Grunberg Rep. 15 ("As of February 2020, the Centers for Disease Control reported more than 2,807 hospitalizations for e-cigarette or vaping associated lung injury ('EVALI') alone and at least 68 deaths in the United States."); Ex. 13, Levy Rep. 21 ("In the literature, these exposures have been reported to cause . . . e-cigarette or vaping associated lung injury (EVALI) as well as chronic lung effects."); Ex. 21, Pue Rep. 20 ("Kleinman et al (2020) reproduced EVALI in an animal model with e-cigarette vaping aerosol exposure without THC or Vitamin E exposure."); Ex. 24, Tackett Rep. 46 ("[T]here are published reports where the person was diagnosed with EVALI and did not report consuming THC products, and there was no vitamin E acetate found in their bronchoalveolar-lavage fluid."); Ex. 25, Winickoff Rep. 35 ("There are also case reports of a rare side effect for young e-cigarette users: hypersensitivity pneumonitis. (CDC reports on EVALI)."); *see also, e.g.*, Ex. 37, Grunberg Dep. 152:25-153:5 ("I believe that JUUL contributed to the number of cases of EVALI."); Ex. 30, Casey Dep. 135:8-135:15 ("It is possible that some of the patients that had EVALI only used Juul."). And Plaintiffs have made potential seizure risks a key part of their case overall. For example, Plaintiffs' class damages expert, Dr. Hal Singer, "focus[ed]" his "Safety-Risk Theory of Harm" on allegations that "Defendants misled Class Members regarding the safety risk of its product, including with respect to cardiovascular and lung injury and disease, ***as well as seizures***" and presented conjoint survey questions based on specific disclaimers regarding "a heightened risk of seizures." *See, e.g.*, Singer Rep. at 3, 9, 17, 22, 76 (ECF No. 1970); Singer Reply Rep. at 21-22, 31-32, 44, 82 (ECF No. 2439).

The Court should rule on the reliability and admissibility of expert opinions regarding EVALI and seizures. JLI believes that Plaintiffs have waived any right to oppose at this stage, but defers to the Court as to the appropriate action in light of Plaintiffs' failure to respond.

2. Asthma.

Plaintiffs' response fails to address Casey's admission that she is not aware of a study finding a causal link between ENDS use and worsening asthma. Ex. 30, Casey Dep. 113:10–17, 152:13–17, 155:2–7, 159:7–12. In the face of this concession from their primary pulmonology expert, Plaintiffs rely on Wills et al. (2021) to link JUUL to asthma use or exacerbation. However, Wills et al. evaluates ENDS products

generally, not JUUL products specifically, and does not conclude that ENDS use causes asthma exacerbation. Tackett and Pue do not present methodology to extrapolate the ENDS data in Wills et al. to JUUL specifically, even though JUUL produces lower carbonyl levels than other ENDS because of its temperature regulation system. Ex. 53, Tackett Dep. 117:18–118:20, 257:13–18. None of the epidemiological studies cited by Plaintiffs' experts establish that JUUL causes asthma exacerbation, nor do Tackett and Pue offer methodology to establish causation through other types of evidence.

Plaintiffs also argue that JLI "cites nothing to contradict these opinions." Pls. Br. at 120. While not required to cite contradictory evidence to succeed on its *Daubert* motion, JLI notes that another epidemiological study Plaintiffs cite in their Opposition, Chaffee et al., *E-Cigarette Use and Adverse Respiratory Symptoms Among Adolescents and Young Adults in the United States*, Prev. Med. 2021, 153, 106766, https://pubmed.ncbi.nlm.nih.gov/34418439/, found that the use of ENDS had no statistically significant association with asthma exacerbation.

3. Other Respiratory Conditions.

Plaintiffs do not even attempt to offer a connection between specific studies or evidence and the "other respiratory conditions" their experts claim are caused by JUUL. Indeed, Tackett and Pue cannot connect any particular constituents of JUUL aerosol with any of these conditions, and they fail to identify reliable or sufficient epidemiological evidence linking the conditions to JUUL use. As Tackett testified, the "other respiratory diseases" referenced are nothing more than the "types of diseases" that the combination of compounds in JUUL aerosol "could cause." Ex. 53, Tackett Dep. 142:11–143:11. Further, Tackett and Pue are not epidemiologists or statisticians, and are not qualified to draw conclusions about population-level patterns of respiratory disease based on an unspecified "mosaic" of sources. Ex. 53, Tackett Dep. 54:5–10, 55:7–20, 223:13–18; Ex. 50, Pue Dep. 166:25–167:5.

4. Exacerbation of GERD.

Plaintiffs do not dispute that there is no epidemiological evidence linking JUUL use to GERD. *Compare* JLI Br. #3 at 20, *with* Pls. Br. at 120. Nor do Plaintiffs dispute that the animal study Winickoff cited (1) did not link the "dose-dependent reduction" in the lower esophageal sphincter to acid reflux in anesthetized opossums, much less in humans; and (2) did not find that reduced LES pressure causes (as opposed to "*may predispose*") humans to GERD. JLI Br. #3 at 20-21.

Plaintiffs' only response is to argue, without citation, that "[n]icotine's relaxing effect on smooth muscles (such as the lower esophageal sphincter) is an established medical fact" well within Winickoff's knowledge. Pls. Br. at 121. Notably, Plaintiffs do not argue that nicotine is capable of causing GERD. *Id*. And Plaintiffs' response fails to show that Winickoff has any basis to reach the next step of his opinion—that nicotine's alleged relaxation on the lower esophageal sphincter is capable of causing GERD, or nicotine at doses present in JUUL is capable of causing GERD. Plaintiffs also argue that JLI's failure to challenge Winickoff's qualifications on the effect of nicotine on the human body somehow makes his opinion stand up to JLI's *Daubert* challenge. Pls. Br. at 121. But whether an expert is qualified is a distinct inquiry from whether that opinion is based upon a reliable scientific methodology. Here, there is no reliable scientific basis for Winickoff to conclude that JUUL use is capable of causing GERD.

C. Plaintiffs Have Failed to Present Reliable Scientific Evidence Regarding the Impact of Addiction on the Developing Brain.

Despite Plaintiffs' say so, Winickoff and Levy fail to present any reliable methodology to support their opinions that adolescent JUUL use can impair brain development. While Plaintiffs contend that Winickoff cites "a myriad of authority to support [his] opinion," Pls. Br. at 121, Plaintiffs fail to specify any such authority beyond the 2016 Surgeon General's Report. And as discussed in JLI's opening brief, the 2016 Surgeon General's Report merely concludes that "[r]odent studies have implications for human adolescents" and that it is ***possible*** that tobacco use during youth affects brain development. Surgeon General's Report 2016 at 107. When extrapolating from this report that JUUL use can impair human adolescent brain development, Winickoff neglects to critically analyze the report's findings and the animal studies that it relies upon—including but not limited to the age the animals were exposed to nicotine and whether the age corresponds to human adolescence, the effects of any stressors on the animals, and the nicotine dosing concentrations and blood nicotine levels. *See In re Prempro Prods. Liab. Litig.*, 738 F. Supp. 2d 887, 894 (E.D. Ark. 2010) ("In addition to the biological differences between species, most animal studies involve significantly higher concentrations of a substance than would ever be present in humans."). This does not mean, as disingenuously stated by Plaintiffs, "only studies that experimented on kids with JUUL would satisfy *Daubert*." Pls. Br. at 122 n.58. But an expert's reliance on animal studies alone is only reasonable if that expert accounts for such variables and provides a reliable basis for

extrapolating from the studies to humans. *See, e.g.*, *Daubert v. Merrell Dow Pharms., Inc.*, 43 F.3d 1311 1314 (9th Cir. 1995) ("*Daubert II*"); *Newkirk*, 727 F. Supp. 2d at 1026. Plaintiffs' experts failed to do so.

Similarly, Plaintiffs are incorrect that "JLI does not elaborate on what studies [cited by Levy] are flawed or how their citation render's [sic] [Levy]'s expert opinion on adolescent brain development unreliable." Pls. Br. at 122 (emphasis omitted). As discussed in JLI's opening brief, Levy bases her opinion solely on studies examining combustible cigarettes—which contain more than a thousand constituents that are not present in JUUL products. And like Winickoff, Levy fails to offer a reliable basis for extrapolating from these studies analyzing the effects of combustible cigarettes to reach her conclusion that JUUL use can impair brain development. In other words, Levy, like Winickoff, makes "too great a leap of faith," *Hall v. Baxter Healthcare Corp.*, 947 F. Supp. 1387, 1411–12 (D. Or. 1996), without offering any explanation for why the results from the studies can be extrapolated to JUUL.

D. Plaintiffs Have Failed to Present Reliable Scientific Evidence Regarding the Psychological Impact of Addiction.

Prochaska, Levy, and Grunberg have failed to present any reliable scientific evidence regarding the purported psychological and behavioral impacts of nicotine addiction, including anxiety disorders, mood disorders, and disruptive behavior disorders. These experts have not offered any study or data to demonstrate that JUUL is the cause of these conditions—disorders which even Levy concedes increase the likelihood of nicotine abuse. Ex. 42, Levy Dep. 37:6–40:7. Although Plaintiffs argue that these experts rely "on a sophisticated analysis of the impact chronic nicotine exposure has on adolescent dopaminergic pathways and limbic systems, and the 'gross neuronal structural changes' that result," Pls. Br. at 122-23 (citation omitted), Plaintiffs—like their experts—fail to explain this supposed "sophisticated analysis" and merely state in a conclusory fashion that "[t]he causal relationship between nicotine and psychological harm" is "established through observational study" and "core neuroscientific understandings," *id*. at 123. Similarly, Plaintiffs' argument that "nicotine addiction worsens the risk of various psychological disorders" and thus "even if certain adolescents [are] predisposed to certain psychological disorders before they use JUUL, the psychological harms flowing from their addiction would still be attributable to JLI" (*id*. at 123) suffers the same deficiencies. A court should not "rely entirely on the experts' unadorned assertions that the methodology they employed comports with standard

scientific procedure," *Daubert II*, 43 F.3d at 1319, and must exclude opinions that are "connected to the underlying data only by the *ipse dixit* of the expert." *Henricksen v. ConocoPhillips Co.*, 605 F. Supp. 2d 1142, 1153 (E.D. Wash. 2009) (citation omitted).

Additionally, Plaintiffs do not refute that Levy's opinion that the presentation of addiction in ENDS users is different (or worse) than in smokers of combustible cigarettes is based solely on her experience treating a single patient for combustible cigarette use. And likewise, Plaintiffs do not refute that this offhand experience treating a single patient does not amount to a reliable scientific basis for her opinion, and thus must be excluded.

III. PLAINTIFFS' RESPONSE CONFIRMS THEIR EXPERTS' CASE-SPECIFIC OPINIONS FAIL TO SATISFY *DAUBERT*.

Plaintiffs argue that the Ninth Circuit's purported "liberal thrust" of the inquiry into the admissibility of specific causation testimony gives Plaintiffs carte blanche to dispense with their *Daubert* obligations. Pls. Br. at 123 (citing *Messick*, 747 F.3d at 1196). Plaintiffs, however, do not dispute that under Ninth Circuit law, an expert must show the injury was "caused by [the defendant's product], rather than some other factor." JLI Br. #3 at 6 (citing *Hardeman*, 997 F.3d at 965 (emphasis added)). Nothing in Plaintiffs' response establishes that Plaintiffs met this requirement for the injuries alleged, or that B.B. in fact suffered from clinically relevant symptoms for certain of her injuries. Instead, Plaintiffs want the Court to admit specific causation opinions that lean so strongly towards the "'art' side of the spectrum" that it dispenses with the science and medicine altogether. Pls. Br. at 123 (citing *In re Roundup*, 358 F. Supp. at 959). *Daubert* does not allow such an outcome.

A. Plaintiffs' Experts' Specific Causation Opinions Lack Reliable Support.

***Asthma*:** Plaintiffs' response confirms that their experts' opinions rely on correlational and temporal conclusions that are conspicuously devoid of actual differential diagnoses or any other methodology to rule out other potential causes. Taken together, none of Plaintiffs' experts provide anything approaching a differential diagnosis of B.B.'s alleged respiratory injuries.

[redacted]

[redacted]

Ex. 54, Winickoff Dep. 32:6-11. Plaintiffs' reliance on Winickoff's general causation report also does not establish specific causation for B.B.

***GERD*:** Plaintiffs' response entirely ignores Winickoff's concession—cited in JLI's opening brief—that he is not aware of any studies looking at whether the severity and frequency of GERD symptoms increase with vaping. JLI Br. #3 at 25. Instead, Plaintiffs respond that Winickoff's methodology is grounded in scientific literature because the scientific literature shows that nicotine loosens the lower esophageal sphincter. Pls. Br. at 137. [redacted] And as discussed above, Winickoff's general causation opinion does not meet *Daubert's* requirements.

[redacted] Winickoff's failure to rule out other potential causes of her GERD exacerbation renders his opinion unreliable.

***Headaches*:** [redacted]

***Depression*:** [redacted]

[redacted]

***Anxiety*:** [redacted]

***Mood Swings*:** Plaintiffs' citation to the generic reports of Winickoff and Prochaska for the proposition that nicotine withdrawal can cause mood swings does not establish that B.B. suffered from mood swings of any clinical significance. Pls. Br. at 131.

[redacted]

***Concentration Issues*:** [redacted]

[redacted]

***Academic/Social Decline*:** [redacted]

B. The Experts' Opinions Regarding Medical Monitoring Lack Reliable Support.

Plaintiffs' response on medical monitoring attempts to relax the standard of admissibility under *Daubert* simply because B.B. no longer has an independent medical monitoring claim. Pls. Br. at 139. Even if B.B. has dropped her independent claim, the bar for admission of expert testimony on medical monitoring damages is not so low that any opinion—even ones that fail to link the medical monitoring Plaintiffs seek to B.B.'s specific risk factors and medical conditions—can find its way to a jury. Plaintiffs point to no authority rebutting the law JLI cited in its opening brief, which requires a showing that the examinations needed are different than what would be prescribed in the absence of exposure or a reasonably necessary consequence of exposure. Regardless, even the Tennessee pattern jury instructions that Plaintiffs cite require Plaintiffs to establish that the "medical care and treatment [is] ***reasonably certain*** to be required in the future." Tenn. P. Civ. Jury Instr. 14.26 (emphasis added). *See also Martinez v. United States*, 2019 WL 266213, at *10 (E.D. Cal. Jan. 18, 2019) (similar).

Plaintiffs' response also does not show that the experts' medical monitoring opinions satisfy *Daubert*. [redacted] And Plaintiffs' response shows only that their experts opine, in general, users of e-cigarette products may develop certain pulmonary, cardiovascular, and mental health

effects. Pls. Br. at 140-41. As discussed above, there is no reliable expert evidence supporting general causation on these points. Nor are any expert's opinions that B.B. herself will need this future medical monitoring based on any reliable methodology, as opposed to speculation that some condition ***might*** befall her at some point in the future. [redacted] Plaintiffs' experts have no reliable basis to opine that she needs more extensive monitoring than she otherwise would receive.

Finally, Plaintiffs wholly fail to respond to JLI's argument on expert opinions regarding B.B.'s alleged future risk of using cigarettes (aside from a one-sentence, unsupported statement in the paragraph about cardiovascular care) and cannabis, and thus, have waived any argument.

CONCLUSION

For the foregoing reasons and those stated in JLI's opening brief, JLI respectfully requests that the Court exclude (i) expert opinions that JUUL, its chemical constituents, or nicotine in JUUL are toxic; (ii) expert opinions on general causation for non-addiction health claims; (iii) expert opinions about the impact of nicotine on the developing brain or the psychological impact of addiction; and (iv) expert opinions on specific causation for B.B.'s non-addiction health claims and medical monitoring damages.

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Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on February 14, 2022, I electronically filed the foregoing document with the Clerk of the Court using the CM/ECF system, which will automatically send notification of the filing to all counsel of record. I also caused a copy of the under-seal documents to be served via electronic mail on all parties.

By: */s/ Renee D. Smith*
Renee D. Smith